

## INVITED COMMENTARY

# The impact of cold ischemia time at the higher end of the KDPI spectrum: what is the risk?

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On December 4, 2014, the new kidney allocation system (KAS) was implemented to reduce extreme longevity mismatches between kidney allograft and recipient life expectancy, increase the highly sensitized patients' access to transplantation through prioritization, broaden access for disadvantaged candidates by counting dialysis time toward wait-list time, and potentially increase the utilization of “marginal kidneys” through broader allocation at the local and regional level. In the first year after implementation, the early results of KAS suggested that the new policies were successful in meeting many of these goals [1]. One casualty of KAS was the increased discard rate of high KDPI organs (KDPI > 85). Another observation was the increase in cold ischemia time (CIT) with the percentage of transplants with CIT >24 h increasing from 18% to 21%. The reasons for this increased discard rate of “marginal kidneys” is likely multifactorial; and certainly, the now quantifiable aspect of a KDPI score may contribute through a “labelling effect” [2]. The role of CIT on expanded criteria donor kidneys has been previously investigated; however, in the setting of the new KAS, increasing CIT may continue to have an even more detrimental effect on organ utilization. To offset this “labeling effect,” it would be of great importance to better understand this donor

population to avoid the unnecessary discard of potentially lifesaving organs.

In this month's issue, Dr. Sampaio *et al.* [3] performed a meta kidney analysis of deceased donor kidney transplants with KDPI  $\geq$  85 donors in the pre-KAS era (2000–2013) from the OPTN/UNOS database. The benefit of this chosen cohort allowed for elimination of the biases created by the “labelling effect” on organ selection in KAS and to establish, based on historical controls, the impact of CIT on post-transplant outcomes. This cohort was divided into three groups for comparison with CIT <12,  $\geq$ 12 to <24, and  $\geq$ 24 h. With a national average of CIT around 18 h, these groups of comparison provide a real-world/real practice scenario for risk stratification in post-transplant outcomes and the spectrum of CIT. The primary conclusions for their analysis were that while there was a trend toward increasing DGF in the longer CIT groups, which achieved statistical significance in the extreme comparison of <12 and  $\geq$ 24 h, there was no statistically significant difference in either patient or graft survival. Interestingly, the authors suggested that the use of mechanical pumping could improve outcomes in these high KDPI kidneys, however, they showed no mitigation of DGF when the CIT  $\geq$ 24 h. Overall these findings are encouraging and suggest that local and regional sharing

of high KDPI kidneys has the advantage of increasing the transplant rates without affecting kidney transplant outcomes. Based on the results of this study, transplant centers should not turn down high KDPI kidneys despite long travel distance as long as the CIT remains within a reasonable range. Sampaio and colleagues would suggest that a CIT  $\geq 24$  h may be a point of deterrence for utilizing these organs in patients more broadly.

The paper also raises multiple important questions. Are all kidneys with KDPI  $\geq 85\%$  the same? Are there differences in DGF rates and transplant outcomes between donation after cardiac death (DCD) and donation after brain death (DBD) kidneys with high KDPI? This study did not subdivide the high KDPI kidneys according to the deceased donor type. It is well known that DCD kidneys are more susceptible to ischemia–reperfusion injury, and it could be possible that the outcomes for high KDPI DCD kidneys are different from DBD kidneys [4]. Another important question is how DGF itself affects transplant outcomes after high KDPI kidney transplantation. This study examined predictors of DGF and kidney transplant outcomes by CIT groups but did not specifically examine the impact of DGF on long-term outcomes. One important message from this paper is that recipient-related factors such as obesity affect high KDPI kidney transplant outcomes, which makes identifying the right recipient critical for achieving the best outcomes for these organs.

As KAS enters its 4th year of implementation, the authors have identified a potential opportunity to improving outcomes in kidney transplant by showing

CIT as a contributor to DGF. As has been previously demonstrated, these high KDPI organs are less likely to be transplanted in the local DSA, and the authors confirm that this distance of travel is the more significant contributor to CIT. Many factors may contribute to this finding—factors such as transplant center behavior, patient selection, and even accepting physician practice. With simultaneous organ offers to regional and local centers, the delay for allocation could potentially be reduced. Also, HLA cross-match testing could be performed prior to donation to reduce any further prolongation of CIT.

While the authors validated the utility of the KDPI stratification by demonstrating reduced long-term graft survival in patients with KDPI  $\geq 85$  donors, they also demonstrated that by accepting a kidney from a KDPI  $\geq 85$  donor, they were also more likely to have a shorter wait time. And so, even in this KDPI  $\geq 85$  donor cohort, their analysis supports the previously proven survival benefit of transplant over time on dialysis [5]. These results should encourage the transplant community for utilizing these “marginal kidneys” in a more strategic way.

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